

Atty. Docket No.: 20200/2093D PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Kreutzer, et al.  
Serial No.: 10/612,179  
Filed: July 2, 2003  
Entitled: METHOD AND MEDICAMENT  
FOR INHIBITING THE  
EXPRESSION OF A GIVEN GENE

Examiner: Not Yet Assigned

Group Art Unit: 1645

Conf. No.: 5239

**CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8a**

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Brenda M. Woods

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*Brenda M. Woods*

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Commissioner for Patents  
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**TRANSMITTAL LETTER**

Enclosed for filing in the above-identified patent application, please find the following documents:

1. Information Disclosure Statement;
2. Form PTO-1449;
3. Copies of Cited References; and
4. Return Post Card.

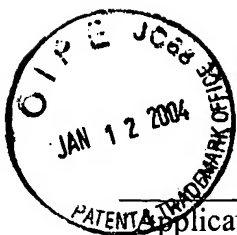
The Commissioner for Patents is hereby authorized to charge any additional fees or credit any overpayment in the total fees to Deposit Account No. 16-0085, Reference No. 20200/2093D. A duplicate of this transmittal letter is enclosed for this purpose.

Respectfully submitted,

Date: January 8, 2004

*Barbara A. Gyure*

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Boston, MA 02199-7613  
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**INFORMATION DISCLOSURE STATEMENT  
UNDER 37 CFR §§ 1.56, 1.97 AND 1.98**

Dear Sir:

In accordance with the duty of disclosure under 37 CFR § 1.56, Applicants submit this Information Disclosure Statement pursuant to 37 CFR §§ 1.97 and 1.98 in the above-identified application for consideration by the Patent Office.

A copy of a portion of the cited documents were submitted to the U.S. Patent and Trademark Office in the parent application, U.S. Serial No. 09/889,802. Copies of the documents in the list which were not submitted with the parent application are enclosed for the Examiner's convenience. Pursuant to CFR § 1.97(b)(3), because this Statement is being submitted before the first Office Action on the merits, no fee is required.

Applicant does not intend to represent that any of the documents submitted herein are material prior art to this invention or that the list represents an exhaustive search of documents related to this invention.

Applicant respectfully requests that the documents submitted herein be considered and made of record in this application.

Respectfully submitted,

Date: January 8, 2004

Name: Barbara A. Cyure

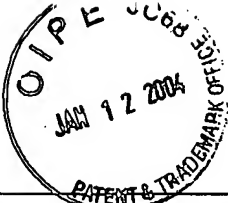
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Patent and Trademark Office

# INFORMATION DISCLOSURE STATEMENT

Attorney Docket No.

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Serial No.

10/612,179

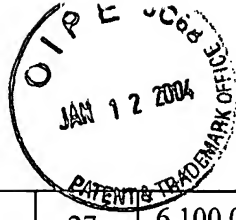
Applicant(s): Kreutzer et al.

Filing Date: July 2, 2003

Group: 1645

## U.S. PATENT DOCUMENTS

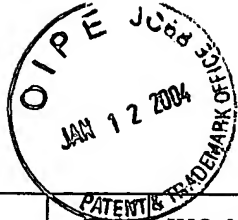
Examiner Initial		Patent No.	Date	Name	Class	Subclass	Filing Date (if appropriate)
	1.	2003/0198627 A1	Oct. 23, 2003	Arts, et al.	424	93.21	Aug. 23, 2002
	2.	2003/0190635 A1	Oct. 9, 2003	McSwiggen	435	6	Jul. 25, 2002
	3.	2003/0180756 A1	Sep. 25, 2003	Shi, et al.	435	6	Nov. 21, 2002
	4.	2003/0176671 A1	Sep. 18, 2003	Reed, et al.	536	23.1	Feb. 7, 2002
	5.	2003/0157030 A1	Aug. 21, 2003	Davis, et al.	424	46	Nov. 4, 2002
	6.	2003/0148341 A1	Aug. 7, 2003	Sin, et al.	435	6	Nov. 5, 2002
	7.	2003/0143732 A1	Jul. 31, 2003	Fosnaugh, et al.	435	325	Aug. 20, 2002
	8.	2003/0125281 A1	Jul. 3, 2003	Lewis, et al.	514	44	May 28, 2002
	9.	2003/0108923 A1	Jun. 12, 2003	Tuschl, et al.	435	6	Sep. 26, 2002
	10.	2002/0086356 A1	Jul. 4, 2002	Tuschl, et al.	435	69.1	Mar. 30, 2001
	11.	6,423,489 B1	Jul. 23, 2002	Anderson, et al.	435	6	May 30, 1995
	12.	6,346,398	Feb. 12, 2002	Pavco, et al.			
	13.	6,355,415	Mar. 12, 2002	Wagner, et al.			
	14.	6,482,803	Nov. 19, 2002	Ruth, et al.			
	15.	6,183,959	Feb. 6, 2001	Thompson			
	16.	6,225,291	May 1, 2001	Lewin, et al.			
	17.	6,245,560	June 12, 2001	Liszewicz			
	18.	6,245,748	June 12, 2001	Wellstein, et al.			
	19.	6,255,071	July 3, 2001	Beach, et al.			
	20.	6,057,156	May 2, 2000	Akhtar, et al.			
	21.	6,071,890	June 6, 2000	Scheule, et al.			
	22.	6,077,705	June 20, 2000	Duane, et al.			
	23.	6,080,851	June 27, 2000	Pachuk, et al.			
	24.	6,087,164	July 11, 2000	Hochberg, et al.			
	25.	6,087,172	July 11, 2000	Veerapaneni, et al.			
	26.	6,099,823	Aug. 8, 2000	Falb			



	27.	6,100,087	Aug. 8, 2000	Rossi, et al.			
	28.	6,100,444	Aug. 8, 2000	Frelinger, et al.			
	29.	6,107,094	Aug. 22, 2000	Crooke			
	30.	5,968,737	Nov. 16, 1999	Ali-Osman , et al.			
	31.	5,985,620	Nov. 16, 1999	Sioud			
	32.	5,908,779	June 1, 1999	Carmichael , et al.			
	33.	5,898,031	Apr 27, 1999	Crooke			
	34.	5,891,717	Apr. 6, 1999	Newgard , et al.			
	35.	5,866,701	Feb. 2, 1999	Hampel , et al.			
	36.	5,864,028	Jan. 26, 1999	Sioud			
	37.	5,854,067	Dec. 29, 1998	Newgard , et al.			
	38.	5,814,500	Nov. 1998	Dietz			
	39.	5,811,300	Nov. 22, 1998	Sullivan , et al.			
	40.	5,811,275	Nov. 22, 1998	Wong-Staal , et al.			
	41.	5,837,510	Nov. 17, 1998	Goldsmith, et al.			
	42.	5,824,519	Oct. 20, 1998	Norris , et al			
	43.	5,712,257	Jan. 1998	Carter			
	44.	5,639,655	June 17, 1997	Thompson, et al.			
	45.	5,635,385	June 3, 1997	Leopold, et al.			
	46.	5,616,459	Apr. 1, 1997	Kramer, et al.			
	47.	5,574,142	Nov. 12, 1996	Meyer, Jr., et al.			
	48.	5,525,468	June 11, 1996	McSwiggen			
	49.	5,496,698	Mar. 5, 1996	Draper , et al.			
	50.	5,246,921	Sep. 21, 1993	Reddy , et al			
	51.	5,225,347	July 6, 1993	Goldberg, et al.			
	52.	5,112,734	May 12, 1992	Kramer, et al.			

#### FOREIGN PATENT DOCUMENTS

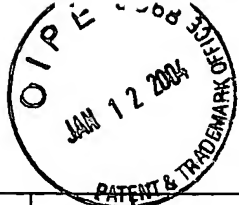
Examiner Initial		Document No.	Publication Date	Country	Class	Subclass	Translation	
							YES	NO
	53.	DE 101 00 586 C1	April 11, 2002	Deutschland (Germany)	C12N	15/11		X
	54.	WO 03/080807 A2	Oct. 2, 2003	PCT	C12N		X	
	55.	WO 03/080794 A2	Oct. 2, 2003	PCT	C12N		X	



56.	WO 03/074654 A2	Sep. 12, 2003	PCT	C12N		X	
57.	WO 03/070972 A2	Aug. 28, 2003	PCT	C12		X	
58.	WO 03/070969 A2	Aug. 28, 2003	PCT	C12Q		X	
59.	WO 03/070750 A2	Aug. 28, 2003	PCT	C07K		X	
60.	WO 03/070283 A2	Aug. 28, 2003	PCT	A61K	48/00	X	
61.	WO 03/016572 A1	Feb. 27, 2003	PCT	C12Q	1/68	X	
62.	WO 03/012052 A2	Feb. 13, 2003	PCT	C12N		X	
63.	WO 02/068637 A2	Sep. 6, 2002	PCT	C12N	15/11	X	
64.	WO 02/068635 A2	Sep. 6, 2002	PCT	C12N	15/11	X	
65.	WO 02/44321 A2	Jun. 6, 2002	PCT	C12N		X	
66.	WO 02/26780 A2	Apr. 4, 2002	PCT	C07K	14/00	X	
67.	WO 01/75164 A2	Oct. 11, 2001	PCT	C12Q	1/68	X	
68.	WO 00/68374	Nov. 16, 2000	PCT	C12N	15/11	X	
69.	WO 00/63364	Oct. 26, 2000	PCT				
70.	WO 00/44895	Aug. 3, 2000	PCT	C12N	15/11		X
71.	WO 00/44914	Aug. 3, 2000	PCT				
72.	WO 00/01846	Jan. 13, 2000	PCT				
73.	WO 99/61631	Dec. 2, 1999	PCT				
74.	WO99/53050	Oct. 21, 1999	PCT				
75.	WO 99/49029	Sept. 30, 1999	PCT				
76.	WO 99 32619	July 1, 1999	PCT				
77.	WO 99/15682	Apr. 1, 1999	PCT				
78.	WO 98/53083	Nov. 26, 1998	PCT				
79.	DE 196 31 919 C2	July 1998	DE			X	
80.	DE 196 18 797 C2	Nov. 13, 1997	DE				X
81.	DE 196 18 797 A1	Oct. 1996	DE			X	
82.	WO94/01550	Jan. 20, 1994	PCT				

OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, etc.)

83.	Agrawal et al., 1995, 105-21, Editors: Akhtar, Saghir, Publisher CRC
84.	Ambros, V., (2001), "Dicing Up RNAs", <i>Science</i> , 293:811-813.
85.	Asanuma, H. et al., (1999), "Photoregulation der Bildung und Dissoziation eines DNA-Duplexes durch <i>cis-trans</i> -Isomerisierung einer Azobenzoleinheit", <i>Angew. Chem.</i> , 111:2547-2549.
86.	Ausubel, F. et al. (1999) Supplement 48, pgs. 9.4.7. to 9.4.8.



87.	Azhayeva, E. et al., (1997), "Inhibitory properties of double helix forming circular oligonucleotides", <i>Nucl. Acids Res.</i> , 25:4954-4961.
88.	Bahramian et al.; MOLECULAR AND CELLULAR BIOLOGY, Vol. 19:274 - 283, "Transcriptional and Posttranscriptional Silencing of Rodent $\alpha 1(I)$ Collagen by a Homologous Transcriptionally Self-Silenced Transgene Jan. 1999
89.	Barwkar, D.A. et al.; Proc. Natl. Acad. Sci USA, Vol. 95:11047 – 11052, September 1998, Chemistry, Biochemistry
90.	Bass, B.L., (2000), "Double-Stranded RNA as a Template for Gene Silencing", <i>Cell</i> , 101:235-238.
91.	Bhan et al., Nucleic Acid Research, 1997; Vol. 25; p. 3310
92.	Billy, et al. (2001) PNAS 98(25):14428-33
93.	Borecky et al. (1981-82) Tex Rep Biol Med 41:575-81 Abstract Only
94.	Castelli, J. et al., (1998), "The 2-5A system in viral infection and apoptosis", <i>Biomed. Pharmacother.</i> , 52:386-390.
95.	Cobaleda, C. et al., (2000), "In vivo inhibition by a site-specific catalytic RNA subunit of Rnase P designed against the BCR-ABL oncogenic products: a novel approach for cancer treatment", <i>Blood</i> , 95(3):731-737.
96.	Datenbank MEDLINE bei STN: AN 1999091059 MEDLINE; DN 99091059 zu: Use of dsRNA-mediated genetic interference to demonstrate that frizzled and frizzled 2 act in the wingless pathway. Kennerdell J.R.; Carthew R.W.; CELL, (1998 Dec. 23) 95(7):1017-1026.
97.	Downward, J. et al., (1990), "Identification of a nucleotide exchange-promoting activity for p21 <sup>ras</sup> ", <i>Proc. Natl. Acad. Sci. USA</i> ", 87:5998-6002.
98.	Elbashir, et al. (2001) Nature 411:494-498
99.	Fire, 9/99, <i>RNA-triggered gene silencing</i> , Trends Genet, 15: 358-363.
100.	Fire, A., et al., 1991, <i>Production of Antisense RNA leads to effective and specific inhibition of gene expression in C. elegans muscle</i> , Development 113: 503-514
101.	Gautschi, O. et al., (2001), "Activity of a Novel bcl-2/bcl-xL-Bispecific Antisense Oligonucleotide Against Tumors of Diverse Histologic Origins", <i>Journal of the National Cancer Institute</i> , 93(6):463-471.
102.	Gibbs, J.B. et al., (1988), "Purification of ras GTPase activating protein from bovine brain", <i>Proc. Natl. Acad. Sci. USA</i> ", 85:5026-5030.
103.	Grasby, JA et al.; Biochemistry 1995 Mar 28; 34(12):4068 – 76
104.	Griffey, RH et al.; J Med Chem 1996 Dec 20; 39(26):5100-9
105.	Ha, I et al.; Genes Dev 1996 Dec 1;10(23):3041-50
106.	Hamilton et al.; SCIENCE, Vol. 286:950 - 951, "A Species of Small Antisense RNA in Posttranscriptional Gene Silencing in Plants (Oct. 29, 1999)
107.	Hammond, S.M. et al., (2000), "An RNA-directed nuclease mediates post-transcriptional gene silencing in <i>Drosophila</i> cells", <i>Nature</i> , 404:293-296.
108.	Hoke, GD et al.; Nucleic Acids Res 1991 Oct 25; 19(20):5743-8

109.	Holen, T. et al., (2002), "Positional effects of short interfering RNAs targeting the human coagulation trigger Tissue Factor", <i>Nucleic Acids Research</i> , 30(8):1757-1766.
110.	Horn, T et al.; <i>Nucleic Acids Research</i> , 1997, Vol. 25, No. 23 : 4842 – 4849
111.	Hunter, 6/17/99, <i>A touch of elegance with RNAi</i> , <i>Curr Biolo</i> , 9: R440-R442
112.	Iwase, R et al.; <i>Nucleic Acids Symp Ser</i> 1997; (37);203 – 4
113.	Jacobs, B.L., and Langland, J.O., 1996, <i>When two stands are better than one: The mediators and modulators of the cellular responses to double-stranded RNA</i> . <i>Virology</i> 219: 339-349
114.	Kennerdell et al.; <i>CELL</i> , Vol. 95, S. 1017 – 1026; "Use of dsRNA-Mediated Genetic Interference to Demonstrate that frizzled and frizzled 2 Act in the Wingless Pathway" Dec 23, 1998
115.	Klemens, et al.(1999), <i>The 2 Å Structure of helix 6 of the human signal recognition particle RNA</i> ., <i>Structure</i> 7(11): 1345-1352
116.	Kreutzer et al (1999) <i>Gesellschaft fur Biochemie und Molekularbiologie</i> S169
117.	Lee, et al.; <i>CELL</i> , Vol. 88; S. 637 – 646; March 7, 1997; "The Cold Shock Domain Protein LIN-28 Controls Developmental Timing in <i>C. elegans</i> and Is Regulated by the lin-4 RNA
118.	Li et al. , <i>Dev. Biology</i> Volume 210, 1999, p. 238 abstract 346
119.	Lin et al.; <i>NATURE</i> , Vol. 402:128 - 129, "Policing rogue genes" Nov. 11, 1999
120.	Lipardi, C. et al., (2001), "RNAi as Random Degradative PCR: siRNA Primers Convert mRNA into dsRNAs that Are Degraded to Generate New siRNAs", <i>Cell</i> , 107:297-307.
121.	Lipinski, et al. (1997) <i>Adv. Drug Delivery Review</i> 23:3-25
122.	Lowy, D.R. et al., (1993), "Function and Regulation of RAS", <i>Annu. Rev. Biochem.</i> , 62:851-891.
123.	Ma MY (1993) <i>Biochem.</i> 32(7):1751-8
124.	Majumdar, A et al.; <i>Nat Genet</i> 1998 Oct; 20(2):212-4
125.	Milhaud et al., <i>Journal of Interferon Research</i> , 1991, vol. 11, 261-265
126.	Minks, M. A. et al., <i>The Journal of Biological Chemistry</i> (1979), 254, (20):10180 – 10183
127.	Montgomery, M., and Fire, 1998, <i>Analysis of a Caenorhabditis elegans twist homolog identifies conserved and divergent aspects of mesodermal patterning</i> , <i>Genes and Development</i> , 12: 2623-2635.
128.	Montgomery M.K., et al., 1998, <i>RNA as a target of double-stranded RNA-mediated genetic interference in Caenorhabditis elegans</i> , <i>Proc. Natl. Acad. Sci.</i> 95: 15502-15507.
129.	Montgomery, et al., July 1998, <i>Double-stranded RNA as a mediator in sequence-specific genetic silencing and co-suppression</i> , <i>TIG</i> , Vol. 14, No. 7., pgs. 255-258
130.	Misquitta, L. and Paterson, B.M., 1999, <i>Targeted disruption of gene function in Drosophila by RNA interference (RNA-i): A role for nautilus in embryonic somatic muscle formation</i> , <i>Proc. Natl. Acad. Sci.</i> 96: 1451-1456
131.	Neilsen et al. (1997) <i>Chem. Comm.</i> 825-826
132.	Ngo, H., et al., 1998, <i>Double-stranded RNA induces mRNA degradation in Trypanosoma brucei</i> , <i>Proc. Natl. Acad. Sci.</i> 95: 14687-14692.
133.	Nikiforov, et al. (1992) <i>Nucleic Acids Research</i> 20(6):1209-1214